UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/100,212	06/19/98	GRAHAM	11525

HM12/0212

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EXAMINER	
KAUFMAN, S	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 02/12/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/100,812	GRAHAM, MICHAEL WAYNE	
	Examiner	Art Unit	
	Sumesh Kaushal	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *6-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 34-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Applicant's response filed on 11/14/00 has been fully considered but is found unpersuasive for the reasons of record as set forth in the earlier office action (Paper No.7, 5/10/00).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application contains claims 6-33 are drawn to an invention nonelected with traverse in Paper No. 6. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 6-33 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 6, filed 04/12/00. Claims 1-4 and 35-45 are pending in this application.

Claim Rejections - 35 USC § 112

Claims 1-4 and 34-45 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, **to make and/or use the invention,** for the same reasons of record as set forth in the official action mailed on 5/10/00.

The applicant argues that the principal feature of the present invention is directed to synthetic genes comprising structural gene sequences, each of which is substantially identical to nucleotide sequence of the target gene, and wherein at least one of structrural gene is placed in the sense orientation relative to the promoter. The applicant further argues that the invention may be applied to down regulate the expression of any target gene in an animal cell (response, page 10, para. 2). The applicant further argues that the invention as claimed is enabled because gene therapy is successful in treating variety of clinical disorders (response, page 10, para. 4). The applicant further argues that claims has been amended to recite downregulation of the expression of a target gene in an animal cell and submits that in the light of specification and prior art those skill in the art are fully enabled to make and use the invention without undue experimentation (response, page 11, para. 2).

However, this is found unpersuasive because the scope of the invention as claimed encompass not only any and all synthetic genes but also its use in the field of gene and/or transgenic animals, wherein any and all synthetic genes are capable of delaying, repressing or reducing the expression of any and all target genes are delayed or repressed.

The invention as claimed encompasses any and all **synthetic genes** or derivatives of target genes. The specification as filed is not enabled because it is not clear what additional sequences may be added, deleted and/or substituted in any target gene to that it qualifies for an art recognized definition of a synthetic gene. Furthermore, the art does not provide an accepted definition for the term gene. Therefore, elaboration of synthetic gene would require both a disclosure of a definition and characterization of the synthetic gene sequence. It is known in the art that different genes have divergent functions. Furthermore, the invention as claimed read upon a combination of multiple gene sequences, wherein the role of each component have not

ascribed. It is not clear how one skilled in the art would use the invention as claimed to modify an unknown target genes in a cell, tissue, organ or an animal.

The earlier office action clearly states that **gene therapy** was regarded as highly unpredictable art because it has been difficult to predict the efficiency and out come of transduced therapeutic genes (Anderson WF, Nature 392:25-30, 1998; Verma et al Nature 389:239-242, 1997). The Recombinant DNA Advisory Committee (RAC) also emphasized that expectations of current gene therapy protocols have been over sold without any apparent success (Touchette, Nat. Med. 2(1) 7-8, 1996, page 7, col.1 para. 2; page 8, col.2 para 1-4). The advisory panel further emphasized the need for a greater understanding of an underlying mechanism that contributes to a genetic disease along with the pathogenesis of the disease. (Touchette, page 7, col.3, para.3). The instant invention is a mere hypothesis wherein a synthetic gene construct is used to delay or repress the expression of a target gene in an animal. The instant specification fails to describe a single working example that demonstrate that the expression of any synthetic gene in an animal via viral or non viral vector results in the delay, repression or reduction any target gene expression.

In addition, the state of **transgenic art** at the time of filing was such that transgene expression and physiological consequences of transgene products in non-mouse mammals are not always accurately predicted among various species of mammals (Wall RJ Theriogenology 45:57-68, 1996). The individual gene of interest, promoter, enhancer, coding or non-coding sequences present in the transgene construct and the site of integration, are the important factors that govern the expression of a transgene (Wall, page 61-62). Furthermore, many biochemical pathways are plastic in nature, which reflects the ability of the embryo to use alternative gene when the preferred gene is modified (Kappel et al. Current Opinion in Biotechnology 3:348-353 1992, page 550, col.1, para. 3-4). In addition, genetic modulation via homologous recombination

is considered highly unpredictable (Viville, in Transgenic Animals, Houdebine (eds), Harwood academic publishers, France. pp307-321, 1997). The specification fails to disclose a single working example, wherein the expression of any synthetic gene (as claimed) results in the delay, repression or reduction of any target gene

To make and test is not the standard for enablement. Therefore, one skill in the art would not exercise the invention as claimed without excessive and undue amount of experimentation. The quantity of experimentation required would include the functional and structural characterization of any and all synthetic gene(s) and their use in the modification of the target gene expression in any and all cell types, tissue types and organisms. The experimentation would also require the development of methods to deliver identified synthetic gene to the target sites for the modification of the target gene expression. The experimentation would also include making of any and all transgenic animals encoding any and all synthetic genes and/or synthetic gene constructs.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Deborah Clark can be reached on (703) 305-4051. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Tracey Johnson, whose telephone number is (703) 308-0377. If the claims are amended canceled and/or added the applicants are advised to follow Amendment Practice under § 1.121 *(http://www.uspto.gov)*.

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